





TECH CENTER 1600/2900

APPENDIX A

Marked-Up Copy of Amendments to Claims

- (Amended) A method for reducing the number of metastases in an animal exhibiting a
 primary tumor comprising administering to said animal a subcytoprotective dose of 10
 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.
- 8. (Amended) The method of claim 1, wherein said [compound] <u>phosphorothioate</u> is an aminoalkylphosphorothioate compound.
- 9. (Amended) The method claim 8, wherein said active derivative of aminoalkylphosphorothioate is the thiol form.
- 10. (Amended) The method claim 8, wherein said active derivative of aminoalkylphosphorothioate is the disulfide form.
- 11. (Amended) The method of claim 1, wherein said [compound] phosphorothioate or active metabolite thereof is selected from the group consisting of WR-2721 (amifostine), WR-1065, WR-638, WR-77913, WR-33278, WR-3689, WR-2822, WR-2529, WR-255591, WR-2823, WR-255709, WR-151326 and WR-151327.
- 12. (Amended) The method of claim 1, wherein [said compound's route of administration is] the route of administration of said phosphorothioate or active metabolite thereof is intravenous, intraperitoneal, intradermal, intramuscularal, dermal, nasal, buccal, rectal, vaginal, inhalation, or topical.
- 13. (Amended) The method of claim 1, wherein said [compound] phosphorothioate or active metabolite thereof is formulated into solutions, suspensions, tablets, pills, capsules, sustained release formulations, powders, creams, ointments, salves, sprays, pumps, liposomes, suppositories, inhalers, and patches.

- 30. (Amended) A method for inhibiting metastasis in an animal exhibiting a primary tumor comprising administering to said animal a subcytoprotective dose of 10 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.
- 31. (Amended) A method for preventing metastasis in an animal exhibiting a primary tumor comprising administering to said animal a subcytoprotective dose of 10 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.

. . . :





APPENDIX B Unofficial Copy Of Claims Currently Pending

- A method for reducing the number of metastases in an animal exhibiting a primary tumor comprising administering to said animal a subcytoprotective dose of 10 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.
- 3. The method of claim 1, wherein the dose is about 10 mg/kg to about 100 mg/kg.
- 4. The method of claim 1, wherein the dose is about 10 mg/kg to about 50 mg/kg.
- 5. The method of claim 1, wherein the dose is about 10 mg/kg to about 25 mg/kg.
- 6. The method of claim 1, wherein said animal is a human.
- 7. The method of claim 1, wherein said tumor is a sarcoma or carcinoma.
- 8. The method of claim 1, wherein said phosphorothioate is an aminoalkylphosphorothioate compound.
- 9. The method claim 8, wherein said active derivative of aminoalkylphosphorothioate is the thiol form.
- 10. The method claim 8, wherein said active derivative of aminoalkylphosphorothioate is the disulfide form.
- 11. The method of claim 1, wherein said phosphorothioate or active metabolite thereof is selected from the group consisting of WR-2721 (amifostine), WR-1065, WR-638, WR-77913, WR-33278, WR-3689, WR-2822, WR-2529, WR-255591, WR-2823, WR-255709, WR-151326 and WR-151327.

- 12. The method of claim 1, wherein the route of administration of said phosphorothioate or active metabolite thereof is intravenous, intraperitoneal, intradermal, intramuscularal, dermal, nasal, buccal, rectal, vaginal, inhalation, or topical.
- 13. The method of claim 1, wherein said phosphorothioate or active metabolite thereof is formulated into solutions, suspensions, tablets, pills, capsules, sustained release formulations, powders, creams, ointments, salves, sprays, pumps, liposomes, suppositories, inhalers, and patches.
- 23. The method of claim 1, further comprising monitoring the ability of the subcytoprotective dose of a phosphorothicate or active metabolite to reduce metastases in the animal.
- 24. The method of claim 23, wherein the monitoring comprises measuring the level of angiostatin stimulation.
- 25. The method of claim 23, wherein the monitoring comprises measuring the level of activity of a matrix metalloproteinase.
- 26. The method of claim 25, wherein the matrix metalloproteinase is MMP-2.
- 27. The method of claim 25, wherein the matrix metalloproteinase is MMP-9.
- 28. The method of claim 23, wherein the monitoring comprising measuring the stimulation of MnSOD.
- 29. The method of claim 28, wherein the measuring of MnSOD stimulation comprises measuring the stimulation of MnSOD gene expression.
- 30. A method for inhibiting metastasis in an animal exhibiting a primary tumor comprising administering to said animal a subcytoprotective dose of 10 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.

31. A method for preventing metastasis in an animal exhibiting a primary tumor comprising administering to said animal a subcytoprotective dose of 10 mg/kg to 150 mg/kg of a phosphorothioate or active metabolite thereof.